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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/520,901

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EXAMINER

SHEN, WU CHENG WINSTON

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/520,901	Applicant(s) FUJIWARA ET AL.	
	Examiner Wu-Cheng Winston Shen	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

This application 10/520,901 is a 371 of PCT/JP03/08573 07/07/2003 claims the foreign priority of JAPAN 2002-198941 filed on 07/08/2002. Preliminary claim amendments filed on 01/07/2005 have been entered

Status of claims: claims 1-11 are currently under examination.

Priority

1. This application is a 371 of PCT/JP03/08573 filed 07/07/2003 claims the foreign priority of JAPAN 2002-198941 filed on 07/08/2002. It is noted that a certified copy of PCT/JP03/08573 in Japanese has been filed for this 371 application. However, no certified copy of JAPAN 2002-198941 filed on 07/08/2002 in either original Japanese or in English translation was provided for instant application. Therefore, without a certified translation of JP 2002-198941, the effective filing date for the instant claims is the filing date of PCT/JP03/08573, 07/07/2003. Applicant cannot rely upon the foreign priority papers to overcome the rejection under 35 USC 102 (e) as set forth below because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

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2. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "A polynucleotide comprising *a promoter from human telomerase* and at least *one E1 gene*". Claims 2-11 depend from claim 1.

It is unclear what the phrase "*a promoter from human telomerase*" encompasses because human telomerase is polypeptide and a promoter is a polynucleotide. It is noted that a promoter cannot be derived from the coding sequences of the recited human telomerase polypeptide sequences.

It is also unclear what the phrase "*one E1 gene*" encompasses. It appears that E1 gene refers to the adenovirus E1 gene as indicated by claim 2, which is a dependent claim of claim 1. However, claim 1 as stated may be interpreted as encompassing any gene whose name has "E1" in it. In this regard, is E1 gene encoding an ubiquitin-activating enzyme involved in both protein degradation and as a target for cancer treatment, encompassed by claim 1?

Claim Rejection - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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3. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of causing cytotoxicity in cancer cells comprising injection, in vitro or in situ, of a vector into a tumor comprising said cancer cells, said vector comprising the hTERT promoter operably linked to a polynucleotide comprising a gene encoding adenovirus E1A followed by an IRES and a gene encoding E1B and for said nucleic acid, does not reasonably provide enablement for 1) a method of treating cancer in vivo, 2) a polynucleotide comprising a promoter from any human telomerase gene or 3) use of the claimed nucleic acid wherein the E1 gene is not operably linked to a promoter to cause expression. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the

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breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The nature of the invention recited in claims 8-11 is directed to a method of treating a cancer comprising using a virus comprising a polynucleotide comprising a promoter from human telomerase and at least one E1 gene. The breadth of claims encompasses treating any cancer either *in vitro* or *in vivo* with any virus comprising a polynucleotide comprising a promoter from human telomerase and at least one E1 gene. It is noted that claims 1-7 are product claims drawn to a nucleic acid. However, the asserted utility of the claimed nucleic acid vector is in treating a cancer, which is not enabled as set forth below.

The claims are not enabled because there is no step recited in the claimed methods. In other words, mere recitation of using the virus comprising a polynucleotide comprising a promoter from human telomerase and at least one E1 gene, does not provide any enabling support of the methods.

With regard to the aspect of administration of a viral polynucleotide for gene therapy, which is encompassed by claims 8-11, it is noted that while progress has been made in recent years for *in vivo* gene transfer, vector targeting *in vivo* to desired sites has continued to be unpredictable and inefficient for the past decade. This statement is supported by numerous teachings available in the art. For example, **Pouton et al.** (Pouton and Seymour, Key issues in non-viral gene delivery, *Adv Drug Deliv Rev.* 46(1-3): 187-203, 2001) reviewed the issues in non-viral gene delivery and stated "direct injection of gene medicines into target tissue represents a far simpler task than targeting delivery to a specific tissue from the systemic circulation". See last full sentence on page 188, right column, and section 2.1. Pouton et al.

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added that there were “no systems yet available for efficient tissue targeting following systemic delivery.” (See page 189, first sentence of section 2.2.). **Johnson-Saliba et al.** stated that although thousands of patients have been involved in clinical trials for gene therapy, using hundreds of different protocols, true success has been limited. A major limitation of gene therapy approaches, especially when non-viral vectors are used, is the poor efficiency of DNA delivery to the nucleus; a crucial step to ensure ultimate expression of the therapeutic gene product (See abstract, Johnson-Saliba et al. Gene therapy: optimizing DNA delivery to the nucleus. *Curr Drug Targets*. 2(4): 371-99, 2001). More recently, **Read et al.** (Read et al., Barriers to gene delivery using synthetic vectors, *Adv Genet*. 53: 19-46, 2005) stated after the time the invention was filed that the “lack of suitable vectors for the delivery of nucleic acids... represents a major hurdle to their continued development and therapeutic application” (see abstract, sentence bridging pages 19 and 20. Problem areas included obtaining persistence in the circulation, gaining access to target cells, and distinguishing target cells from non-target cells. See e.g. page 22). Finally, **Dobson** (Dobson, Gene therapy progress and prospects: magnetic nanoparticle-based gene delivery. *Gene Ther*. 13(4): 283-7, 2006) reviewed the development of non-viral transfection agents for gene delivery stated “While magnetic targeting appears to hold significant potential for gene therapy, there are still major obstacles to employing this technique in the clinic. Perhaps, the problem that is most difficult to overcome is, as with magnetic targeting for drug delivery, that of scale-up.” (See Prospects on page 286).

The specification teaches administration of the claimed vector to cells in vitro and tumors implanted in mice (i.e. in situ), resulting in cytotoxicity of the cancer cells. The specification does not teach treatment of a cancer in vivo. As stated in the preceding section,

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there is lack of predictability in the art regarding transport of a polynucleotide, which encodes a polypeptide of therapeutic interest. For instance, the route of administration to targeted cells of certain tissue, the transport of polynucleotide into nucleus for transcription to occur, and the expression level required for desired therapeutic effects are among those critical factors need to be addressed for gene therapy. In the absence of information disclosed regarding specific polynucleotide for certain targeted gene therapy purpose, a skilled person in the art cannot make and use of the gene therapy approach for treating a cancer without undue experimentation. It is unpredictable regarding whether the conditions work for a specific polynucleotide encoding a particular polypeptide may be directly extrapolate to another polynucleotide encoding another polypeptide to achieve the therapeutic effect of interest, which is encompassed by the scope of claims 8-11 of instant application.

The specification only discloses infecting cancer cells that are transplanted into a mouse, which is not equivalent to treating a cancer in a mammal. However, the specification does not disclose that E1 alone will kill the cells. Furthermore, the specification does not disclose any other vector than adenovirus and any other promoter than hTERT promoter. Finally the specification does not disclose how one would administer the vector to a patient to treat cancer as discussed in the prior arts.

In summary, the specification does not provide any guidance regarding how the recited virus is to be utilized for treating a cancer. The specification fails to provide information regarding, for instance, (i) what are the genes to be expressed by hTERT promoter, (ii) what are the routes of administration of the recited virus, (iii) what are the technical considerations required for initiation of the expression of a given therapeutic gene of interest and sustenance of

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sufficient expression level for treating a given cancer of interest, and (iv) how are the immune responses resulting from introduction of adenovirus minimized in term of what part of adenovirus genome of the recited adenovirus remained in addition to the recited E1 gene. In the absence of relevant information, there is lack of predictability if the recited method can treat a cancer. An artisan is left to perform undue experimentation to sort out the feasibility of making and using the claimed invention.

In view of the state of the art, the unpredictability in the art, and the lack of specific guidance and working examples in the specification, one of skill in the art would have to perform undue experimentation to make and use the claimed invention as recited in claims 1-11.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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4. Claims 1-3, 5-8 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Morin et al. (Morin et al., 2000, WO 00/46355, international publication date, August 10, 2000; this reference is disclosed in IDS filed on 04/25/2006, listed as reference No. BA).

It is noted that Morin et al. disclosed the information encompassed by the claimed invention of the instant application. However, neither Morin et al. nor instant application provides enabling support of gene therapy in treating a cancer, for the claimed inventions. It is further noted that different interpretations of claims can be applied to the rejections under 35 U.S.C. 102 and the rejection 35 U.S.C. 112 first paragraph pertaining to enablement issue. Therefore, there is no contradiction between the art rejection stated here and the rejection under 35 U.S.C 112, first paragraph.

Morin et al., 2000 disclosed that telomerase reverse transcriptase is part of the telomerase complex responsible for maintaining telomere length and increasing the replicative capacity of progenitor cells. Telomerase activity is turned off in mature differentiated cells, but is turned back on again in hyperplastic diseases, including many cancers. The disclosure by Morin et al., 2000 provides regulatory elements that promote transcription in cells that express telomerase reverse transcriptase (TERT). Morin et al., 2000 also described oncolytic viruses, in which a toxin or a genetic element essential for viral replication is placed under control of the TERT promoter. Thereby, the virus replicates preferentially in cells expressing TERT, and selectively lyses cancer cells.

With regard to adenovirus, adenovirus derived E1 gene, and human telomerase reverse transcriptase (TERT) promoter (claims 2, 3, 5, and 6 of instant application), Morin et al., 2000 teach a series of constructs showing construction of oncolytic adenovirus, made conditionally

replicative by placing the E1a replication under control of an hTERT promoter (See lines 14-15, page 4, and Figure 5, Morin et al., 2000).

With regard to adenovirus as an anticancer agent and a method of treating a cancer comprising using the said adenovirus as an anticancer agent (claims 7, 8, and 11 of instant application), Morin et al., 2000 teach a method of treating a subject for a disease, including a cancer, associated with increased expression of TERT in affected cells, comprising administering to the subject an effective amount of the oncolytic adenovirus (See claims 23-26, page 47, Morin et al., 2000). It is noted that a pharmaceutically acceptable carrier, excipient or diluent recited in claim 7 of instant application reads on water for diluting recited adenoviral vectors performed by Morin et al., 2000.

Thus, Morin et al., 2000 clearly anticipates the claims 1-3, 5-8, and 11 of instant invention.

5. Claims 1-3 and 5-11 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Cheng et al. (Cheng et al., U.S. patent application No. 2003/0104625, publication date, June 5, 2003; filed Feb. 22, 2002).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

It is noted that Cheng et al. disclosed the information encompassed by the claimed invention of the instant application. However, neither Cheng et al. nor instant application provides enabling support of gene therapy for treating a cancer, for the claimed inventions. It

is further noted that different interpretations of claims can be applied to the rejections under 35 U.S.C. 102 and the rejection 35 U.S.C. 112 first paragraph pertaining to enablement issue. Therefore, there is no contradiction between the art rejection stated here and the rejection under 35 U.S.C 112, first paragraph.

Cheng et al., 2003 teach oncolytic adenoviral vectors and their use in methods of gene therapy (See title and abstract, Cheng et al., 2003).

With regard to adenovirus, adenovirus derived E1 gene, and human telomerase reverse transcriptase (TERT) promoter (claims 2, 3, 5, 6 of instant application), Cheng et al., 2003 teach a series of constructs showing construction of oncolytic adenovirus, made conditionally replicative by placing the E1a replication under control of an hTERT promoter (See lines 14-15, page 4, and Figure 5, Morin et al., 2000). The diagram of a series of constructs includes Ar17pAE2fTtex (Figure 48, Cheng et al., 2003) and the diagram indicates the known transcription factor binding sites are indicated above each added promoter. Briefly, a modified E1 gene is driven by the E2F-1 promoter and a human telomerase reverse transcriptase (hTERT) promoter is driving the E4 transcription unit (See paragraphs [0059]-[0061], page 4, and Figure 48, 49 and 50, Cheng et al., 2003).

With regard to adenovirus as an anticancer agent and a method of treating a cancer comprising using the said adenovirus as an anticancer agent (claims 7, 8, and 11 of instant application of instant application), Cheng et al., 2003 teach a method of selectively killing a neoplastic cell in a cell population which comprises contacting a cell an effective amount of the disclosed adenoviral vector with human telomerase reverse transcriptase (hTERT) promoter and modified E1 gene (See claim 52, Cheng et al., 2003). It is noted that a pharmaceutically

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acceptable carrier, excipient or diluent recited in claim 7 of instant application reads on water for diluting recited adenoviral vectors performed by Cheng et al., 2003.

With regard to treating a type of cancer using adenovirus as an anticancer agent (claims 9 and 10 of instant applicant), Cheng et al. teach tumor and normal tissues, including liver, kidney, lung, bone marrow, brain, spleen, and ovary, were collected from various experimental mice groups three days after administration of adenoviral vector (See paragraph [0570], Cheng et al., 2003).

Thus, Cheng et al., 2003 clearly anticipates the claims 1-3 and 5-11 of instant invention.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al. (Morin et al., 2000, WO 00/46355, international publication date, August 10, 2000; this reference is disclosed in IDS filed on 04/25/2006, listed as reference No. BA) taken with Li et al. (Li et al., A hepatocellular carcinoma-specific adenovirus variant, CV890, eliminates distant human liver tumors in combination with doxorubicin. *Cancer Res.* 61(17): 6428-36, 2001; this reference is disclosed in IDS filed on 04/25/2006, listed as reference No. CC) .

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Morin et al., 2000 disclosed that telomerase reverse transcriptase is part of the telomerase complex responsible for maintaining telomere length and increasing the replicative capacity of progenitor cells. Telomerase activity is turned off in mature differentiated cells, but is turned back on again in hyperplastic diseases, including many cancers. The disclosure by Morin et al., 2000 provides regulatory elements that promote transcription in cells that express telomerase reverse transcriptase (TERT). Morin et al., 2000 also described oncolytic viruses, in which a toxin or a genetic element essential for viral replication is placed under control of the TERT promoter. Thereby, the virus replicates preferentially in cells expressing TERT, and selectively lyses cancer cells.

With regard to adenovirus, adenovirus derived E1 gene, and human telomerase reverse transcriptase (TERT) promoter, Morin et al., 2000 teach a series of constructs showing construction of oncolytic adenovirus, made conditionally replicative by placing the E1a replication under control of an hTERT promoter (See lines 14-15, page 4, and Figure 5, Morin et al., 2000).

However, Morin et al. do not teach an adenovirus with IRES inserted between E1A and E1B in an adenovirus as recited in claim 4 of instant application.

At the time the claimed invention was made, the bicirtronic cassette in an adenovirus 5 vector (Ad5), E1A-IRES (internal ribosome entry site)-E1B, was known in the art for translational control of E1A and E1B expression. For instance, Li et al. teach devised a strategy for the control an artificial E1A-IRES-E1B bicistronic cassette in an adenovirus 5 vector (Ad5) and constructed an **hepatocellular carcinoma(HCC)**-specific oncolytic adenoviruses, CV890. CV890 efficiently replicates in and destroys AFP-producing HCC cells as well as wild-type Ad5,

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but replication is highly attenuated in non-AFP-producing HCC cells or non-HCC cells (See abstract, Li et al., 2001).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Morin et al., regarding the cell and tissue specificity of hTERT promoter and its transcriptional regulation in an adenovirus with the teachings of Li et al. regarding a bicistronic cassette in an adenovirus 5 vector (Ad5) harboring E1A gene, an IRES sequence, and an E1B arranged in E1A-IRES-E1B order and the translational regulation by IRES. One having ordinary skill in the art would have been motivated to combine the teachings of Morin et al. and Li et al. because hTERT promoter taught by Morin et al. activate transcription in specifically in tumor cells and IRES taught by Li et al. in an Ad5 vector controlling the expression of E1A and E1B at translational level.

There would have been a reasonable expectation of success given (i) successful identification human TERT promoter and demonstration of hTERT promoter driven reporter gene expression at transcription level by the teachings of Morin et al. and (ii) the successful construction and expression from the E1A-IRES-E1B construct by the teachings of Li et al., and its translational regulation of E1A and E1B expression exerted by IRES

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

7. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

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application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio, Ph.D./

Primary Examiner

AU 1632

Wu-Cheng Winston Shen, Ph. D.

Patent Examiner

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